



DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA-2021-D-1214]

Considerations for the Use of Real-World Data and Real-World Evidence to Support Regulatory Decision-Making for Drug and Biological Products; Guidance for Industry; Availability

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice of availability.

SUMMARY: The Food and Drug Administration (FDA or Agency) is announcing the availability of a final guidance for industry entitled “Considerations for the Use of Real-World Data and Real-World Evidence to Support Regulatory Decision-Making for Drug and Biological Products.” FDA is issuing this guidance as part of its Real-World Evidence (RWE) Program for drugs and to satisfy, in part, the mandate under the Federal Food, Drug, and Cosmetic Act (FD&C Act) to issue guidance about the use of RWE in regulatory decision making. This guidance discusses the applicability of FDA’s investigational new drug application (IND) regulations to various clinical study designs that utilize real-world data (RWD) and clarifies the Agency’s expectations regarding clinical studies using RWD submitted to FDA in support of a regulatory decision regarding the effectiveness or safety of a drug that are not subject to the IND regulations. This guidance finalizes the draft guidance of the same title issued on December 9, 2021.

DATES: The announcement of the guidance is published in the *Federal Register* on [INSERT DATE OF PUBLICATION IN THE *FEDERAL REGISTER*].

ADDRESSES: You may submit either electronic or written comments on Agency guidances at any time as follows:

Electronic Submissions

Submit electronic comments in the following way:

- Federal eRulemaking Portal: <https://www.regulations.gov>. Follow the instructions for submitting comments. Comments submitted electronically, including attachments, to <https://www.regulations.gov> will be posted to the docket unchanged. Because your comment will be made public, you are solely responsible for ensuring that your comment does not include any confidential information that you or a third party may not wish to be posted, such as medical information, your or anyone else's Social Security number, or confidential business information, such as a manufacturing process. Please note that if you include your name, contact information, or other information that identifies you in the body of your comments, that information will be posted on <https://www.regulations.gov>.
- If you want to submit a comment with confidential information that you do not wish to be made available to the public, submit the comment as a written/paper submission and in the manner detailed (see "Written/Paper Submissions" and "Instructions").

Written/Paper Submissions

Submit written/paper submissions as follows:

- Mail/Hand delivery/Courier (for written/paper submissions): Dockets Management Staff (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852.
- For written/paper comments submitted to the Dockets Management Staff, FDA will post your comment, as well as any attachments, except for information submitted, marked and identified, as confidential, if submitted as detailed in "Instructions."

Instructions: All submissions received must include the Docket No. FDA-2021-D-1214 for "Considerations for the Use of Real-World Data and Real-World Evidence to Support Regulatory Decision-Making for Drug and Biological Products." Received comments will be placed in the docket and, except for those submitted as "Confidential Submissions," publicly

viewable at <https://www.regulations.gov> or at the Dockets Management Staff between 9 a.m. and 4 p.m., Monday through Friday, 240-402-7500.

- Confidential Submissions--To submit a comment with confidential information that you do not wish to be made publicly available, submit your comments only as a written/paper submission. You should submit two copies total. One copy will include the information you claim to be confidential with a heading or cover note that states “THIS DOCUMENT CONTAINS CONFIDENTIAL INFORMATION.” The Agency will review this copy, including the claimed confidential information, in its consideration of comments. The second copy, which will have the claimed confidential information redacted/blacked out, will be available for public viewing and posted on <https://www.regulations.gov>. Submit both copies to the Dockets Management Staff. If you do not wish your name and contact information to be made publicly available, you can provide this information on the cover sheet and not in the body of your comments and you must identify this information as “confidential.” Any information marked as “confidential” will not be disclosed except in accordance with 21 CFR 10.20 and other applicable disclosure law. For more information about FDA’s posting of comments to public dockets, see 80 FR 56469, September 18, 2015, or access the information at:
<https://www.govinfo.gov/content/pkg/FR-2015-09-18/pdf/2015-23389.pdf>.

Docket: For access to the docket to read background documents or the electronic and written/paper comments received, go to <https://www.regulations.gov> and insert the docket number, found in brackets in the heading of this document, into the “Search” box and follow the prompts and/or go to the Dockets Management Staff, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852, 240-402-7500.

You may submit comments on any guidance at any time (see 21 CFR 10.115(g)(5)).

Submit written requests for single copies of this guidance to the Division of Drug Information, Center for Drug Evaluation and Research, Food and Drug Administration, 10001

New Hampshire Ave., Hillandale Building, 4th Floor, Silver Spring, MD 20993-0002; or to the Office of Communication, Outreach and Development, Center for Biologics Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 71, Rm. 3128, Silver Spring, MD 20993-0002. Send one self-addressed adhesive label to assist that office in processing your requests. See the SUPPLEMENTARY INFORMATION section for electronic access to the guidance document.

FOR FURTHER INFORMATION CONTACT: Dianne Paraoan, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 51, Rm. 3226, Silver Spring, MD 20993-0002, 301-796-3161, Dianne.Paraoan@fda.hhs.gov; or Anne Taylor, Center for Biologics Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 71, Rm. 7301, Silver Spring, MD 20993-0002, 240-402-7911, Anne.Taylor@fda.hhs.gov.

SUPPLEMENTARY INFORMATION:

I. Background

FDA is announcing the availability of a guidance for industry entitled “Considerations for the Use of Real-World Data and Real-World Evidence to Support Regulatory Decision-Making for Drug and Biological Products.” The guidance discusses the following major topics: (1) applicability of 21 CFR part 312 to studies using RWD and (2) regulatory considerations for non-interventional (observational) studies involving the use of RWD. Regulatory considerations addressed by the guidance include the following: (1) transparency for data collection and analysis, (2) access to RWD, (3) study monitoring, (4) safety reporting, (5) other sponsor responsibilities, and (6) the analysis of RWD generated from the use of a product under an emergency use authorization (EUA) in routine practice.

Section 3022 of the 21st Century Cures Act (Cures Act) of 2016 amended the FD&C Act to add section 505F, Utilizing Real World Evidence (21 U.S.C. 355g), which requires FDA to issue guidance about the use of RWE in regulatory decision-making. In addition, under the

Prescription Drug User Fee Amendments of 2017 (PDUFA VI), FDA is committed to publish draft guidance on how RWE can contribute to the assessment of safety and effectiveness in regulatory submissions. In 2018, FDA created an RWE Framework and an RWE Program to evaluate the potential use of RWE to help support the approval of a new indication for a drug already approved under the FD&C Act or to help support or satisfy postapproval study requirements. In late 2021, FDA utilized the RWE Program to issue draft guidances outlining considerations for the use of RWD and RWE in regulatory decision making to satisfy the Cures Act mandate and the PDUFA VI commitment.

This guidance finalizes the draft guidance of the same title issued on December 9, 2021 (86 FR 70131). FDA considered comments received on the draft guidance as the guidance was finalized. Changes from the draft to the final guidance include transfer of relevant definitions from the glossary to the text as well as additional language about data generated in clinical practice for products used under an EUA consistent with a mandate under the Food and Drug Omnibus Reform Act of 2022. Clarifying information was also added, including the use of existing regulatory pathways for third parties to provide patient-level data to FDA when a sponsor cannot submit such data to FDA through traditional channels. In addition, editorial changes were made to improve clarity.

This guidance is being issued consistent with FDA's good guidance practices regulation (21 CFR 10.115). The guidance represents the current thinking of FDA on "Considerations for the Use of Real-World Data and Real-World Evidence to Support Regulatory Decision-Making for Drug and Biological Products." It does not establish any rights for any person and is not binding on FDA or the public. You can use an alternative approach if it satisfies the requirements of the applicable statutes and regulations.

II. Paperwork Reduction Act of 1995

While this guidance contains no collection of information, it does refer to previously approved FDA collections of information. The previously approved collections of information

are subject to review by Office of Management and Budget (OMB) under the Paperwork Reduction Act of 1995 (PRA) (44 U.S.C. 3501-3521). The collections of information in 21 CFR part 11 pertaining to electronic records and signatures have been approved under OMB control number 0910-0303. The collections of information in 21 CFR parts 50 and 56 relating to protection of human subjects and Institutional Review Boards have been approved under OMB control number 0910-0130. The collections of information in 21 CFR part 310 relating to postmarketing adverse drug experience reporting have been approved under OMB control number 0910-0230. The collections of information in 21 CFR part 600 for general records and postmarketing adverse experience reporting pertaining to biological products have been approved under OMB control number 0910-0308. The collections of information in 21 CFR parts 310, 314, and 600 pertaining to adverse event and product experience reporting have been approved under OMB control number 0910-0291. The collections of information in 21 CFR part 312 have been approved under OMB control number 0910-0014. The collections of information in 21 CFR part 314 have been approved under OMB control number 0910-0001. The collections of information in 21 CFR part 601 have been approved under OMB control number 0910-0338. The collections of information in 21 CFR part 600 have been approved under OMB control number 0910-0458.

III. Electronic Access

Persons with access to the internet may obtain the guidance at:

<https://www.fda.gov/drugs/guidance-compliance-regulatory-information/guidances-drugs>,
<https://www.fda.gov/vaccines-blood-biologics/guidance-compliance-regulatory-information-biologics/biologics-guidances>, <https://www.fda.gov/regulatory-information/search-fda-guidance-documents>, or <https://www.regulations.gov>.

Dated: August 28, 2023.

Lauren K. Roth,

Associate Commissioner for Policy.

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